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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/676,391

10/01/2003

Daniel Kahne

PUAM-0258

9155

23377 7590 04/20/2007

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EXAMINER

LUNDGREN, JEFFREY S

ART UNIT

PAPER NUMBER

1639

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

04/20/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

# Office Action Summary

Application No.

10/676,391

Applicant(s)

KAHNE ET AL.

Examiner

Jeff Lundgren

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 1/10/07.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 42-49 and 57-73 is/are pending in the application.
- 4a) Of the above claim(s) 57-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 42-49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 42-49 and 57-73 are pending in the instant application; claims 57-73 are withdrawn from consideration; claims 42-49 are the subject of the Office Action below.

### ***Objection to the Abstract - Withdrawn***

The objection to the Abstract is withdrawn in view of Applicants' amendment.

### ***Claim Rejections - 35 USC § 112, first paragraph (Scope of Enablement)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 42-49 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement beyond the relative scope of the working examples, is maintained in modified form in view of Applicants' amendment to the claims. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, Applicants have not demonstrated the claimed reaction chemistry on a protected glycopeptide that "has no free amino or carboxyl groups and has a free hydroxyl group only at the 6-position." For example, see reaction Scheme I prior to paragraph 0069. The vancomycin compound in this scheme has other free hydroxyls, and a free amino group. The breadth for groups Ar and G is reasonably supported.

The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands* (USPQ 2d 1400: CAFC 1988) which include: a) The breadth of the claims; b) the nature of the invention; c) the state of the prior art; d) the level of one of ordinary skill; e) The level of predictability in the art; f) The amount of direction provided by the inventor; g) The presence or absence of working examples; and h) the quantity of experimentation necessary needed to make or use the invention based on the disclosure; See *In re Wands* USPQ 2d 1400 (CAFC 1988).

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*The breadth of the claims*

The breadth of potential glycopeptides of different chemical structure as encompassed by claim 42 is unsupported in light of the failure to substantially teach compounds as broadly as claimed.

*The nature of the Invention/State of the Prior art*

The present invention is directed to the making and screening of glycopeptide antibiotics; although it is noted that claims 1 and 102 are not so limited. Additionally, it is noted that “the nature and placement of the sugars on the glycopeptide antibiotics play critical roles in antibiotic activity”. In this regard it is further noted that, “that there have been no reports of modification on the glucose residues of vancomycin which have affected activity” E.g. see specification page 7, first full paragraph.

*The level of one of ordinary skill*

The level of one of ordinary skill in the art is high, and would likely encompass a person having earned a MS or Ph.D. with at least a few years experience following their degree.

*The level of predictability in the art*

The sugar residues of the vancomycin and other glycopeptide antibiotics have been shown to affect binding activities e.g. “the nature and placement of the sugars on the glycopeptide antibiotics play critical roles in antibiotic activity”. Additionally, structural changes in the sugar residues can produce significant changes in antibiotic activity. See e.g. specification page 4, first full paragraph. Accordingly, the making and potential usefulness of “glycopeptide” compounds of different chemical structure is not a priori predictable. Courts have recognized that reaction steps or compound structure which is shown to be (e.g. by applicant or prior art) to be critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976); *Ex parte Bhide* (BdPatApp&Int) 42 USPQ2d 14.

For example, on pages 970-972, *Pace* (*Pace et al.*, *Biochemical Pharmacology* 71:968-980 (2006)) shows how even the smaller class of vancomycin compounds have unpredictable activities, let alone the largely diverse claimed core by Applicants:

“The goal of the project that culminated in the discovery of oritavancin was to improve over vancomycin’s pharmacokinetic properties, and was

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based on an understanding of the relevant structure–activity relationship differences between vancomycin and teicoplanin. Improvements in alkylated and acylated analogs of vancomycin were deemed inadequate, and other natural product glycopeptides were subsequently evaluated as platforms [108–111]. Compounds like chloreremomycin (LY264826) exhibiting better activity and spectrum were utilized as a starting point, and eventually leads were evolved to the resultant chlorobiphenyl-modified lipoglycopeptide that is oritavancin.”

Pace, page 970, col. 2 (emphasis added).

Also, specifically regarding Applicants elected species, Li (Li *et al.*, *Curr. Pharm. Design* 11:3111-3124 (2005)) teaches how the vancomycin compounds have distinctly unique properties:

“Based on the above mechanism, several research groups have devised different approaches that circumvent the low affinity bindings between vancomycin and D-Ala-D-Lac. Kahne *et al.* synthesized modified carbohydrates that are analogs of the aminoglycoside part of the vancomycin. These compounds exhibited good activity against vancomycin resistant microorganisms. *They suggested that these carbohydrate derivatives function by a different mechanism, in which the modified carbohydrates interact directly with bacterial proteins involved in the transglycosylation step of the cell wall biosynthesis and do not require the binding of terminal peptides for activity* [30]. Later, they used these sets of small molecules to discover the genes that help to regulate the transglycosylation step of peptidoglycan synthesis and established a genetic basis for activity differences between their compounds and vancomycin [31].”

Li, pages 3112 to 3113 (emphasis added).

*The amount of direction/working examples*

The specification only provides guidance and examples directed to the making and use (e.g. antibiotic) of vancomycin glucose C6 substituted derivatives which share a common structure which is not representative of the scope of claimed glycopeptides. See Example 7.

*Quantity of Experimentation*

In light of the unpredictability surrounding the making and use of glycopeptide derivatives of diverse structure which possess antibiotic activity, the undue breadth of the claimed invention, the lack of adequate guidance regarding the making and antibiotic testing of a representative sample of glycopeptides, the lack of exemplified compounds bearing reasonable

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art-accepted substituents, the lack of critical/essential core structure, one wishing to practice the presently claimed invention would be unable to do so without engaging in undue experimentation.

***Claim Rejections - 35 USC § 112, first paragraph (Written Description)***

The rejection of claims 42-49 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained in modified form in view of Applicants' amendment to the claims. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.*

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Specifically, Applicants have not demonstrated the claimed reaction chemistry on a protected glycopeptide that "has *no* free amino or carboxyl groups and has a free hydroxyl group *only* at the 6-position." For example, see reaction Scheme I before paragraph 0069. The vancomycin compound in this scheme has other free hydroxyls, and a free amino group. The breadth for groups Ar and G is reasonably supported.

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For example, on pages 970-972, Pace (Pace *et al.*, *Biochemical Pharmacology* 71:968-980 (2006)) shows how even the smaller class of vancomycin compounds have unpredictable activities, let alone the largely diverse claimed core by Applicants:

“The goal of the project that culminated in the discovery of oritavancin was to improve over vancomycin’s pharmacokinetic properties, and was based on an understanding of the relevant structure–activity relationship differences between vancomycin and teicoplanin. ***Improvements in alkylated and acylated analogs of vancomycin were deemed inadequate***, and other natural product glycopeptides were subsequently evaluated as platforms [108–111]. Compounds like chloreremomycin (LY264826) exhibiting better activity and spectrum were utilized as a starting point, and eventually leads were evolved to the resultant chlorobiphenyl-modified lipoglycopeptide that is oritavancin.”

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Also, specifically regarding this compound class and Applicants elected species, Li (Li *et al.*, *Curr. Pharm. Design* 11:3111-3124 (2005)) teaches how these vancomycin compounds have distinctly unique properties:

“Based on the above mechanism, several research groups have devised different approaches that circumvent the low affinity bindings between vancomycin and D-Ala-D-Lac. Kahne et al. synthesized modified carbohydrates that are analogs of the aminoglycoside part of the vancomycin. These compounds exhibited good activity against vancomycin resistant microorganisms. ***They suggested that these carbohydrate derivatives function by a different mechanism, in which the modified carbohydrates interact directly with bacterial proteins involved in the transglycosylation step of the cell wall biosynthesis and do not require the binding of terminal peptides for activity*** [30]. Later, they used these sets of small molecules to discover the genes that help to regulate the transglycosylation step of peptidoglycan synthesis and established a genetic basis for activity differences between their compounds and vancomycin [31].”

Li, pages 3112 to 3113 (emphasis added).

Accordingly, one of ordinary skill in the art would not accept Applicants claimed genus as being supported by the instant disclosure.

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### ***Conclusions***

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsius verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

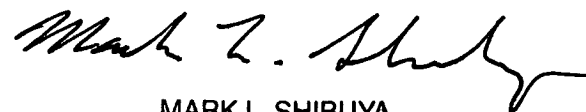
If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Schultz, can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL



MARK L. SHIBUYA  
PRIMARY EXAMINER